

SEQUENCE LISTING

<110> Merck & Co., Inc.
Istituto di Ricerche di Biologia Molecolare P. Angeletti S.p.A.

<120> HCV REPLICONS CONTAINING NS5B FROM
GENOTYPE 2B

<130> 21564Y PCT

<150> 60/517,605

<151> 2003-11-05

<160> 28

<170> FastSEQ for Windows Version 4.0

<210> 1

<211> 591

<212> PRT

<213> Artificial Sequence

<220>

<223> modified NS5B

<221> VARIANT

<222> (5)...(5)

<223> Xaa = threonine or serine

<221> VARIANT

<222> (24)...(24)

<223> Xaa = asparagine or serine

<221> VARIANT

<222> (31)...(31)

<223> Xaa = methionine or isoleucine

<221> VARIANT

<222> (376)...(376)

<223> Xaa = isoleucine or leucine

<400> 1

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			20					25					30		
Phe	His	Asn	Lys	Val	Tyr	Ser	Thr	Thr	Ser	Arg	Ser	Ala	Ser	Leu	Arg
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Ala	Lys	Lys	Val	Thr	Phe	Asp	Arg	Val	Gln	Val	Leu	Asp	Ala	His	Tyr
		50				55				60					
Asp	Ser	Val	Leu	Gln	Asp	Val	Lys	Arg	Ala	Ala	Ser	Lys	Val	Ser	Ala
65				70					75					80	
Arg	Leu	Leu	Thr	Val	Glu	Glu	Ala	Cys	Ala	Leu	Thr	Pro	Pro	His	Ser
				85					90					95	

Ala	Lys	Ser	Arg	Tyr	Gly	Phe	Gly	Ala	Lys	Glu	Val	Arg	Ser	Leu	Ser	100	105	110
Arg	Arg	Ala	Val	Asn	His	Ile	Arg	Ser	Val	Trp	Glu	Asp	Leu	Leu	Glu	115	120	125
Asp	Gln	His	Thr	Pro	Ile	Asp	Thr	Thr	Ile	Met	Ala	Lys	Asn	Glu	Val	130	135	140
Phe	Cys	Ile	Asp	Pro	Thr	Lys	Gly	Gly	Lys	Lys	Pro	Ala	Arg	Leu	Ile	145	150	155
Val	Tyr	Pro	Asp	Leu	Gly	Val	Arg	Val	Cys	Glu	Lys	Met	Ala	Leu	Tyr	165	170	175
Asp	Ile	Ala	Gln	Lys	Leu	Pro	Lys	Ala	Ile	Met	Gly	Pro	Ser	Tyr	Gly	180	185	190
Phe	Gln	Tyr	Ser	Pro	Ala	Glu	Arg	Val	Asp	Phe	Leu	Leu	Lys	Ala	Trp	195	200	205
Gly	Ser	Lys	Lys	Asp	Pro	Met	Gly	Phe	Ser	Tyr	Asp	Thr	Arg	Cys	Phe	210	215	220
Asp	Ser	Thr	Val	Thr	Glu	Arg	Asp	Ile	Arg	Thr	Glu	Glu	Ser	Ile	Tyr	225	230	235
Gln	Ala	Cys	Ser	Leu	Pro	Gln	Glu	Ala	Arg	Thr	Val	Ile	His	Ser	Leu	245	250	255
Thr	Glu	Arg	Leu	Tyr	Val	Gly	Gly	Pro	Met	Thr	Asn	Ser	Lys	Gly	Gln	260	265	270
Ser	Cys	Gly	Tyr	Arg	Arg	Cys	Arg	Ala	Ser	Gly	Val	Phe	Thr	Thr	Ser	275	280	285
Met	Gly	Asn	Thr	Met	Thr	Cys	Tyr	Ile	Lys	Ala	Leu	Ala	Ala	Cys	Lys	290	295	300
Ala	Ala	Gly	Ile	Val	Asp	Pro	Val	Met	Leu	Val	Cys	Gly	Asp	Asp	Leu	305	310	315
Val	Val	Ile	Ser	Glu	Ser	Gln	Gly	Asn	Glu	Glu	Asp	Glu	Arg	Asn	Leu	325	330	335
Arg	Ala	Phe	Thr	Glu	Ala	Met	Thr	Arg	Tyr	Ser	Ala	Pro	Pro	Gly	Asp	340	345	350
Leu	Pro	Arg	Pro	Glu	Tyr	Asp	Leu	Glu	Leu	Ile	Thr	Ser	Cys	Ser	Ser	355	360	365
Asn	Val	Ser	Val	Ala	Leu	Asp	Ser	Arg	Gly	Arg	Arg	Arg	Tyr	Phe	Leu	370	375	380
Thr	Arg	Asp	Pro	Thr	Thr	Pro	Xaa	Thr	Arg	Ala	Ala	Trp	Glu	Thr	Val	385	390	395
Arg	His	Ser	Pro	Val	Asn	Ser	Trp	Leu	Gly	Asn	Ile	Ile	Gln	Tyr	Ala	405	410	415
Pro	Thr	Ile	Trp	Val	Arg	Met	Val	Ile	Met	Thr	His	Phe	Phe	Ser	Ile	420	425	430
Leu	Leu	Ala	Gln	Asp	Thr	Leu	Asn	Gln	Asn	Leu	Asn	Phe	Glu	Met	Tyr	435	440	445
Gly	Ala	Val	Tyr	Ser	Val	Asn	Pro	Leu	Asp	Leu	Pro	Ala	Ile	Ile	Glu	450	455	460
Arg	Leu	His	Gly	Leu	Glu	Ala	Phe	Ser	Leu	His	Thr	Tyr	Ser	Pro	His	465	470	475
Glu	Leu	Ser	Arg	Val	Ala	Ala	Thr	Leu	Arg	Lys	Leu	Gly	Ala	Pro	Pro	485	490	495
Leu	Arg	Ala	Trp	Lys	Ser	Arg	Ala	Arg	Ala	Val	Arg	Ala	Ser	Leu	Ile	500	505	510
Ala	Gln	Gly	Ala	Arg	Ala	Ala	Ile	Cys	Gly	Arg	Tyr	Leu	Phe	Asn	Trp	515	520	525

Ala	Val	Lys	Thr	Lys	Leu	Lys	Leu	Thr	Pro	Leu	Pro	Glu	Ala	Ser	Arg
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Leu	Asp	Leu	Ser	Gly	Trp	Phe	Thr	Val	Gly	Ala	Gly	Gly	Gly	Asp	Ile
545					550					555					560
Tyr	His	Ser	Val	Ser	His	Ala	Arg	Pro	Arg	Leu	Leu	Leu	Leu	Cys	Leu
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<210> 2

<211> 1776

<212> DNA

<213> Artificial Sequence

<220>

<223> modified NS5B

<221> variation

<222> (3)...(3)

<223> n = A or T

<221> variation

<222> (9)...(9)

<223> n = C or A

<221> variation

<222> (13)...(13)

<223> n = A or T

<221> variation

<222> (15)...(15)

<223> n = A or C

<221> variation

<222> (21)...(21)

<223> n = A or G

<221> variation

<222> (24)...(24)

<223> n = C or G

<221> variation

<222> (28)...(28)

<223> n = T or C

<221> modified_base

<222> (30)...(30)

<223> n = G or C

<221> variation

<222> (33)...(33)

<223> n = C or A

<221> variation

<222> (71)...(71)

<223> n = A or G

<221> variation

<222> (83)...(83)

<223> n = G or T

<221> variation

<222> (1174)...(1174)

<223> n = A or C

<400> 2

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<210> 3

<211> 1394

<212> PRT

<213> Artificial Sequence

<220>

<223> modified NS3-5A

<221> VARIANT

<222> (1215)...(1215)

<223> Xaa = asparagine or serine

<221> VARIANT

<222> (904)...(904)

<223> Xaa = valine or alanine

<400> 3

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Glu Val Gln Val Val Ser Thr Ala Thr Gln Ser Phe Leu Ala Thr Cys
          35          40          45
Val Asn Gly Val Cys Trp Thr Val Tyr His Gly Ala Gly Ser Lys Thr
          50          55          60
Leu Ala Gly Pro Lys Gly Trp Pro Ile Thr Gln Met Tyr Thr Asn Val Asp
65          70          75          80
Gln Asp Leu Val Gly Trp Gln Ala Pro Pro Gly Ala Arg Ser Leu Thr
          85          90          95
Pro Cys Thr Cys Gly Ser Ser Asp Leu Tyr Leu Val Thr Arg His Ala
          100          105          110
Asp Val Ile Pro Val Arg Arg Arg Gly Asp Ser Arg Gly Ser Leu Leu
          115          120          125
Ser Pro Arg Pro Val Ser Tyr Leu Lys Gly Ser Ser Gly Gly Pro Leu
          130          135          140
Leu Cys Pro Ser Gly His Ala Val Gly Ile Phe Arg Ala Ala Val Cys
145          150          155          160
Thr Arg Gly Val Ala Lys Ala Val Asp Phe Val Pro Val Glu Ser Met
          165          170          175
Glu Thr Thr Met Arg Ser Pro Val Phe Thr Asp Asn Ser Ser Pro Pro
          180          185          190
Ala Val Pro Gln Thr Phe Gln Val Ala His Leu His Ala Pro Thr Gly
          195          200          205
Ser Gly Lys Ser Thr Lys Val Pro Ala Ala Tyr Ala Ala Gln Gly Tyr
          210          215          220
Lys Val Leu Val Leu Asn Pro Ser Val Ala Ala Thr Leu Gly Phe Gly
225          230          235          240
Ala Tyr Met Ser Lys Ala His Gly Ile Asp Pro Asn Ile Arg Thr Gly
          245          250          255
Val Arg Thr Ile Thr Thr Gly Ala Pro Val Thr Tyr Ser Thr Tyr Gly
          260          265          270
Lys Phe Leu Ala Asp Gly Gly Cys Ser Gly Gly Ala Tyr Asp Ile Ile
          275          280          285
Ile Cys Asp Glu Cys His Ser Thr Asp Ser Thr Thr Ile Leu Gly Ile
          290          295          300
Gly Thr Val Leu Asp Gln Ala Glu Thr Ala Gly Ala Arg Leu Val Val
305          310          315          320
Leu Ala Thr Ala Thr Pro Pro Gly Ser Val Thr Val Pro His Pro Asn
          325          330          335
Ile Glu Glu Val Ala Leu Ser Asn Thr Gly Glu Ile Pro Phe Tyr Gly
          340          345          350
Lys Ala Ile Pro Ile Glu Ala Ile Arg Gly Gly Arg His Leu Ile Phe
          355          360          365
Cys His Ser Lys Lys Lys Cys Asp Glu Leu Ala Ala Lys Leu Ser Gly
          370          375          380
Leu Gly Ile Asn Ala Val Ala Tyr Tyr Arg Gly Leu Asp Val Ser Val
385          390          395          400

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Ile	Pro	Thr	Ile	Gly	Asp	Val	Val	Val	Val	Ala	Thr	Asp	Ala	Leu	Met
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			420					425					430		
Val	Thr	Gln	Thr	Val	Asp	Phe	Ser	Leu	Asp	Pro	Thr	Phe	Thr	Ile	Glu
		435					440					445			
Thr	Thr	Thr	Val	Pro	Gln	Asp	Ala	Val	Ser	Arg	Ser	Gln	Arg	Arg	Gly
	450					455					460				
Arg	Thr	Gly	Arg	Gly	Arg	Met	Gly	Ile	Tyr	Arg	Phe	Val	Thr	Pro	Gly
465					470					475					480
Glu	Arg	Pro	Ser	Gly	Met	Phe	Asp	Ser	Ser	Val	Leu	Cys	Glu	Cys	Tyr
			485					490						495	
Asp	Ala	Gly	Cys	Ala	Trp	Tyr	Glu	Leu	Thr	Pro	Ala	Glu	Thr	Ser	Val
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Arg	Leu	Arg	Ala	Tyr	Leu	Asn	Thr	Pro	Gly	Leu	Pro	Val	Cys	Gln	Asp
	515						520					525			
His	Leu	Glu	Phe	Trp	Glu	Ser	Val	Phe	Thr	Gly	Leu	Thr	His	Ile	Asp
	530					535					540				
Ala	His	Phe	Leu	Ser	Gln	Thr	Lys	Gln	Ala	Gly	Asp	Asn	Phe	Pro	Tyr
545					550					555					560
Leu	Val	Ala	Tyr	Gln	Ala	Thr	Val	Cys	Ala	Arg	Ala	Gln	Ala	Pro	Pro
			565					570						575	
Pro	Ser	Trp	Asp	Gln	Met	Trp	Lys	Cys	Leu	Ile	Arg	Leu	Lys	Pro	Thr
		580						585					590		
Leu	His	Gly	Pro	Thr	Pro	Leu	Leu	Tyr	Arg	Leu	Gly	Ala	Val	Gln	Asn
	595					600						605			
Glu	Val	Thr	Leu	Thr	His	Pro	Ile	Thr	Lys	Tyr	Ile	Met	Ala	Cys	Met
	610					615					620				
Ser	Ala	Asp	Leu	Glu	Val	Val	Thr	Ser	Thr	Trp	Val	Leu	Val	Gly	Gly
625					630					635					640
Val	Leu	Ala	Ala	Leu	Ala	Ala	Tyr	Cys	Leu	Thr	Thr	Gly	Ser	Val	Val
			645						650					655	
Ile	Val	Gly	Arg	Ile	Ile	Leu	Ser	Gly	Arg	Pro	Ala	Ile	Val	Pro	Asp
		660						665					670		
Arg	Glu	Phe	Leu	Tyr	Gln	Glu	Phe	Asp	Glu	Met	Glu	Glu	Cys	Ala	Ser
	675						680					685			
His	Leu	Pro	Tyr	Ile	Glu	Gln	Gly	Met	Gln	Leu	Ala	Glu	Gln	Phe	Lys
	690					695					700				
Gln	Lys	Ala	Leu	Gly	Leu	Leu	Gln	Thr	Ala	Thr	Lys	Gln	Ala	Glu	Ala
705					710					715					720
Ala	Ala	Pro	Val	Val	Glu	Ser	Lys	Trp	Arg	Ala	Leu	Glu	Thr	Phe	Trp
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Ala	Lys	His	Met	Trp	Asn	Phe	Ile	Ser	Gly	Ile	Gln	Tyr	Leu	Ala	Gly
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Leu	Ser	Thr	Leu	Pro	Gly	Asn	Pro	Ala	Ile	Ala	Ser	Leu	Met	Ala	Phe
	755					760						765			
Thr	Ala	Ser	Ile	Thr	Ser	Pro	Leu	Thr	Thr	Gln	Ser	Thr	Leu	Leu	Phe
	770					775					780				
Asn	Ile	Leu	Gly	Gly	Trp	Val	Ala	Ala	Gln	Leu	Ala	Pro	Pro	Ser	Ala
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Ala	Ser	Ala	Phe	Val	Gly	Ala	Gly	Ile	Ala	Gly	Ala	Ala	Val	Gly	Ser
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Gly	Val	Ala	Gly	Ala	Leu	Val	Ala	Phe	Lys	Val	Met	Ser	Gly	Glu	Met		
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Pro	Ser	Thr	Glu	Asp	Leu	Val	Asn	Leu	Leu	Pro	Ala	Ile	Leu	Ser	Pro		
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Gly	Ala	Leu	Val	Val	Gly	Val	Val	Cys	Ala	Ala	Ile	Leu	Arg	Arg	His		
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Val	Gly	Pro	Gly	Glu	Gly	Ala	Val	Gln	Trp	Met	Asn	Arg	Leu	Ile	Ala		
				885					890						895		
Phe	Ala	Ser	Arg	Gly	Asn	His	Xaa	Ser	Pro	Thr	His	Tyr	Val	Pro	Glu		
			900					905					910				
Ser	Asp	Ala	Ala	Ala	Arg	Val	Thr	Gln	Ile	Leu	Ser	Ser	Leu	Thr	Ile		
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Thr	Gln	Leu	Leu	Lys	Arg	Leu	His	Gln	Trp	Ile	Asn	Glu	Asp	Cys	Ser		
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Thr	Pro	Cys	Ser	Gly	Ser	Trp	Leu	Arg	Asp	Val	Trp	Asp	Trp	Ile	Cys		
945					950					955					960		
Thr	Val	Leu	Thr	Asp	Phe	Lys	Thr	Trp	Leu	Gln	Ser	Lys	Leu	Leu	Pro		
				965					970						975		
Gln	Leu	Pro	Gly	Val	Pro	Phe	Phe	Ser	Cys	Gln	Arg	Gly	Tyr	Lys	Gly		
			980					985					990				
Val	Trp	Arg	Gly	Asp	Gly	Ile	Met	Gln	Thr	Thr	Cys	Pro	Cys	Gly	Ala		
		995					1000					1005					
Gln	Ile	Thr	Gly	His	Val	Lys	Asn	Gly	Ser	Met	Arg	Ile	Val	Gly	Pro		
		1010				1015					1020						
Lys	Thr	Cys	Ser	Asn	Thr	Trp	His	Gly	Thr	Phe	Pro	Ile	Asn	Ala	Tyr		
1025					1030					1035					1040		
Thr	Thr	Gly	Pro	Cys	Thr	Pro	Ser	Pro	Ala	Pro	Asn	Tyr	Ser	Arg	Ala		
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Leu	Trp	Arg	Val	Ala	Ala	Glu	Glu	Tyr	Val	Glu	Val	Thr	Arg	Val	Gly		
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Asp	Phe	His	Tyr	Val	Thr	Gly	Met	Thr	Thr	Asp	Asn	Val	Lys	Cys	Pro		
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Cys	Gln	Val	Pro	Ala	Pro	Glu	Phe	Phe	Thr	Glu	Val	Asp	Gly	Val	Arg		
		1090				1095					1100						
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Thr	Phe	Gln	Val	Gly	Leu	Asn	Gln	Tyr	Leu	Val	Gly	Ser	Gln	Leu	Pro		
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Cys	Glu	Pro	Glu	Pro	Asp	Val	Ala	Val	Leu	Thr	Ser	Met	Leu	Thr	Asp		
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Thr	Arg	Val	Glu	Ser	Glu	Asn	Lys	Val	Val	Val	Leu	Asp	Ser	Phe	Asp		
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 Pro Pro Ile Pro Pro Pro Arg Arg Lys Arg Thr Val Val Leu Thr Glu
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<210> 4
 <211> 4182
 <212> DNA
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<220>
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<221> variation
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 <223> n = T or C

<221> variation
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 <223> n = A or G

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15/15